THE ASSOCIATION BETWEEN SERUM URIC ACID CONCENTRATION AT PRESENTATION AS AN INDICATOR OF OUTCOME AMONG ACUTE ISCHAEMIC STROKE

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CERTIFICATE

This is to certify that the thesis entitled **THE ASSOCIATION BETWEEN SERUM URIC ACID CONCENTRATION AT PRESENTATION AS AN INDICATOR OF OUTCOME AMONG ACUTE ISCHAEMIC STROKE** is a bonafide work of **Dr.M.S.MAHMOOD SULAIMAN**, done under my direct guidance and supervision in the department of General Medicine, PSG Institute of Medical Sciences & Research, Coimbatore in fulfillment of the regulations of Tamilnadu Dr.MGR Medical University for the award of MD degree in General Medicine.

GUIDE & HOD **PRINCIPAL**

DECLARATION

I hereby declare that this dissertation entitled was prepared by me under the direct guidance and supervision of professor **Dr. K. JAYACHANDRAN MD, Dr.BALAKRISHNAN MD, DM**, PSG Institute of Medical Sciences & Research, Coimbatore.

The dissertation is submitted to the Tamilnadu Dr.MGR Medical University in fulfillment of the University regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for the award of any other Degree or Diploma.

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AIM

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INTRODUCTION

For many years uric acid, has been used in clinical practice as a marker of severe metabolic disturbances. Its antioxidant property has not been considered for a very long time.

The plasma concentration of uric acid is almost 10-fold higher than other antioxidants such as Vitamin C and Vitamin E. It is considered that uric acid has much higher antioxidant capacity[1.] Uric acid which is formed by catabolism of purine is proposed to neutralize the free radical injury that occurs in ischemic stroke.

Epidemiological studies have suggested a direct relationship between the levels of the natural antioxidant uric acid and the risk of cerebrovascular and coronary ischaemic events.[2, 3] However it is not completely clear whether this association indicates that uric acid is an independent ischaemic risk factor or it represents a marker of atherosclerotic disease. Whether the concentration of uric acid at the onset of ischaemic symptoms influences the severity of stroke also remains to be elucidated.

REVIEW OF LITERATURE

Stroke or cerebrovascular accident by definition of WHO is a rapidly developing clinical symptoms and/or signs of focal neurological deficit and at times global loss of cerebral function(coma) lasting longer than 24 hrs or leading to death with no apparent cause other than vascular origin [4].

The 24 hours threshold in the definition excludes transient ischaemic attacks (TIA).

Stroke includes a number of syndromes with differing etiologies, epidemiology, prognosis and treatment. These are listed in the WHO's international classification of diseases (1975)

a. Sub arachnoid haemorrhage – 1-2%
b. Cerebral haemorrhage – 10%
c. Cerebral thrombosis or embolism – 85%
d. Occlusion of precerebral arteries
e. Transient cerebral ischaemia of more than 24 hours
f. III defined cardiovascular disease (i.e., underlying pathology in brain is not determined.

Stroke is a world wide health problem making an important contribution to morbidity, mortality and disability in developed as well as in developing countries.

Cerebral thrombosis is usually the most frequent form of stroke encountered in clinical studies, though there are substantial differences in frequency from place to place. Subarachnoid haemorrhage and cerebral embolism come next, as regards both mortality or morbidity.

Cerebral ischaemia is caused by a reduction in blood flow that lasts for a several seconds to few minutes. Neurologic symptoms are manifest within 10 sec because neurons lack glycogen and suffer rapid energy failure. This cerebral ischaemia or infarction is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart.

The caused of ischaemia-infarction are:

ISCHAEMIC STROKE

a. **Thrombotic – 25%**
   - i. Lacunar stroke - 20-25%
   - ii. Large vessel - 1-5%

b. **Embolic - 75%**
   - i. Cardio embolic - 20%
   - ii. Artery – Artery - 15%
   - iii. Cryptogenic - 30%
   - iv. Other - 10%

PATHOPHYSIOLOGY OF CEREBRAL ISCHAEMIA

The Brain is an obligatory aerobe. It derives its energy from the oxidative metabolism of glucose. There are only negligible stores of glucose in the brain. So when the cerebral blood flow falls and the brain becomes ischaemic a series of functional and neurophysiological changes, which are dependent on the oxidative metabolism of glucose to provide energy in the form of ATP occurs at various thresholds of flow.[5]

The normal cerebral blood flow (CBF) in man is 50ml/100 gms of brain/min. Using Positron Emission Tomography, the cerebral energy metabolism is measured as cerebral metabolic rate of oxygen ($CMRO_2$) and of glucose (CMR glu). It has also been studied that the oxygen extraction fraction (OEF) remains the same throughout the brain.[6] Therefore in resting normal human brain; the CBF is a reliable reflection of $CMRO_2$.

In ischaemia when CBF falls below about 20ml/100g/min, [7] the oxygen extraction fraction becomes maximal and the $CMRO_2$ begins to fall. Infact a high OEF is only seen early after acute ischaemic stroke, in the first day or so.

If flow is restored, functional recovery is still possible. At this stage, lactate production increases due to ineffective anaerobic metabolism of glucose. The pH falls and ATP synthesis is impaired. As flow falls further, energy – dependent functions of the cell membranes becomes progressively affected. Water Sodium and Chloride enters the cells. Calcium also enters and Potassium (K^+) leaks out.[8] Cellular transport mechanisms and neurotransmitter systems fail.Certain potentially neurotoxic transmitters are released such as L-glutamate. The oxygen radicals and lipid peroxides are formed. So damaging cells further.[9] Neurons start releasing PAF, (Platelet Activating Factor) which may be neurotoxic.

When the blood flow falls further less than 10ml/100gm/min, infarction occurs and even if flow is restored function does nor recover. At this stage, the $CMRO_2$ and CBF is low and OEF will be normal indicating the pure metabolic depression. Sometimes the OEF may be low indicating the CBF is in excess of requirements for the low metabolic demands of the infracted tissue. It is called luxury perfusion. In absolute luxury perfusion, CBF is increased which is termed as hyper perfusion.

The consequences of the fall in CBF depend not just on the depth of ischaemia, but also on its duration. In focal ischaemia, flow is almost never reduced to zero because of the collateral blood supply which is therefore, a further factor in determining the metabolic consequences. The local CBF may also be influenced by the development of cerebral edema and raised intracranial pressure. Acid metabolites and the increasing extra cellular potassium concentrations cause vasodilatation. Vasoconstrictor prostaglandins are released from aggregating platelets and damaged cell membranes.

Blood viscosity and aggregation of formed elements slow the microcirculation and eventually thrombosis. The metabolic consequences of ischaemia may be exacerbated in the presence of high prevailing glucose concentration. But the worst outcome may be related to the hyperglycemia of stress response and reflect the severity of initial stroke.[11] When the lactate levels are increased, seizures may occur.

Systemic hypoxia (as a consequence of pneumonia etc) and dehydration, increasing the hematocrit and blood viscosity are further exacerbating factors.

Damaged brain may also have impaired responses to $PACO_2$ and PaO_2 as well as impaired auto regulation and perfusion reserve. This makes the brain very sensitive to any further insults such as systemic hypoxia, hypotension and raised intracranial pressure.

FREE RADICAL DAMAGE

Ischaemia induced free radical damage is most likely to occur if ischaemia is followed by recirculation. This occurs because oxygen radicals are formed when reduced compound which is accumulated during ischaemia is reoxidised. However free radical production can occur at relatively low oxygen tensions and can be triggered by the accumulation of reduced compounds.

Ischaemia promotes the conversion of Xanthine Dehydrogenase (XDH) to Xanthine Oxidase (XO). A rise in calcium may activate proteases which favours this conversion. Whereas XDH activity does nor produces reactive oxygen species, the XO reaction is a major source of free redicals during ischaemia reperfusion injury.

$$\text{Hypoxanthine} + O_2 \rightarrow \text{Xanthine} + O_2 + H_2O_2$$

$$\text{Xanthine} + O_2 \rightarrow \text{Uric acid} + O_2 + H_2O_2$$

Another source of free radicals is Nitric Oxide. O_2 and NO decompex to form toxic peroxynitrate ion (NO_3) No synthetase is also stimulated by the rising calcium levels in the ischaemic tissue.

Uric acid, its mono-anion urate (at physiological $_pH$ values) is traditionally considered to be a metabolic inert end product of purine metabolism in man without any physiological value.

Uric acid is implicated in various pathological conditions such as Gout, Lesch- Nyhan syndrome, Xanthinuria etc. However, this ubiquituous compound has proven to be a selective anti oxidant, capable especially of reaction with hydroxyl radicals and hypochlorous acid. It also gets converted to innocuous products (allantoin, allantoate, glyoxalate, urea, and oxalate). There

is now evidence for such processes not only in vitro in isolated organs but also in human lung in vivo. Urate may also serve as an

Oxidiable co-substrate for the enzyme cyclooxygenase. The major site of urate production as shown for coronary system is the mircovascular endothelium in isolated organ preparations. Urate is shown to protect against reperfusion damage induced by activated granulocytes and cells known to produce a variety of radicals and oxidants. Intriguingly, urate prevents oxidative inactivation of endothelial enzymes (cyclooxygenase, Angiotensin Converting Enzymes) preserves the ability of the endothelium to mediate vascular dilatation in the face of the oxidative stress. This suggests a particular relationship between the site of urate formation and the need for a biologically potent free radical scavenger and auto oxidant.

Risk factors for cerebral infarction

1. Unmodifiable risk factors
2. Major modifiable risk factors
3. Questionable rare or weak modifiable risk factors.
4. Risk factors predominant in the young

RISK FACTORS FOR CEREBRAL INFARCTION

Unmodifiable risk factors	Questionable, rare, or weak modifiable risk factors	Risk factors predominant in the young
Age	AIDS	Mitral valve leaflet Prolapse
Sex	Alcohol	Sickle cell disease and Other hemoglobinopathies
Race	Fibrinogen and platelets	Migraine
Family history	Lipids	Cocaine abuse
Previous stroke	Exercise	Obstructive sleep apnea
Major modifiable Risk factors	Hematocrit	Intercurrent infection
Atrial fibrillation	Water supply	Patent foramen ovale
Hypertension	Anticardiolipin antibodies	Atrial septal aneurysm
	Oral contraceptives	
Isolated systolic hypertension	Pregnancy	System lupus erythematosus
Myocardial infarction	Homocystinuria	
Other heart disease	Diet	
Diabetes mellitus	Socioeconomic status	
Transient ischemic attacks	Season, Claudication	
Smoking		

1. UNMODIFIABLE RISK FACTORS

a. **Age**

Age is the single most powerful risk factor for cerebral infarction. Since the increase with age is exponential, doubling or tripling with every decade after the fifth. [13]

b. **Sex**

Mortality rates for men are 23% to 115% higher than for women in all countries.[14]

c. **Race**

There is generally a higher incidence of all strokes types and cerebral infarction in blacks. [15]

d. **Previous stroke**

The recurrence rate of cerebral infarction is 10-30%. The first 6 months is the period of highest risk.[16] Hypertension, Diabetes and Smoking increase the risk, while an infarction of undetermined cause is associated with a diminished risk.

2. Modifiable risk factors

a. **Atrial Fibrillation**

Atrial fibrillation causes 20% of all infarcts[17] and is associated with a relative risk of death from stroke of 12.25[18]. Silent infarcts are found in 20% more of the population with atrial fibrillation and this is exacerbated by increasing age and left atrial diameter.[19]

b.

c. **Hypertension**

After age, hypertension is the most powerful risk factor for cerebral infarction. Both systolic and diastolic pressures are important. Sex differences are not prominent in analyses of the effects of hypertension on stroke. Prolonged treatment of diastolic BP to produce a fall of 6mm Hg decreases the stroke risk by 40% and the benefits accure within 3 years.[20]

d. **Myocardial infarction**

Cerebral infarction occurs in between 1% and 1.25% of cases within 1 years after myocardial infaction.[21] Transmural infarcts pose a greater risk than sybendocardial infarcts. A history of myocardial infarction is also a risk factor for cerebral infarction.[22]

e. **Other Heart Disease**

Cardiac disease in general doubles the risk of stroke. While left ventricular hypertrophy quadruples it, independent of hypertension.[23] Cardiac failure, coronary Heart disease and angina increases the risk of cerebral infarction.

f. **Diabetes Mellitus**

Though variable, the evidence now supports diabetes as a risk factor for stroke.[24] Impaired glucose tolerance may be a risk factor and an elevated glycosylated hemoglobin may be found in upto 42% patients with cerebral infarcts not previously known to have diabetes.

g.

h. **Transient Ischaemic Attacks**

The incidence of stroke increases after TIA. The relative risk of stroke after TIA is 13.4 in the first 12 months and 7 over first 7 years.[25]

g. Smoking

Smoking is one of the most important risk factors. There is A dose response relationship, the risk doubling in the heaviest of smokers.[26] In the Framingham study, cessation of smoking removed the additional risk of stroke within 2 years.

g. **Alcohol**

The effect of a alcohol on cerebral infarction has two aspects. These being sudden heavy (binge) drinking and chronic consumption. There is evidence for an association between sudden heavy drinking and the onset of cerebral infarction in young adults.[27] Chronic light alcohol intake is associated with a decreases risk of stroke.[26] Chronic heavy consumption 180 -400g/wk is associated with an increased risk.

i. Lipids

Total cholesterol has a weak association with cerebral infarction. Framingham study suggest a weak correlation between cholesterol and triglycerides and the risk of Atherothrombotic brain infarction.

j. **Exercise**

Lack of exercise may increase the risk of all stroke in women.[28]

MINOR FACTORS

Soft water has been associated with an increased risk (7%) of death from stroke according to death certificates.

Anti Cardio Lipin antibodies are associated with increased risk for cerebral infarction.Homocystinuria is a recognized high risk factor for stroke.

Acquired Immuno Deficiency Syndrome (AIDS) is a risk factor for infarction. The previse mechanism is unknown, but an associated CNS infection typically with Cryptococcus species, tuberculosis or varicella zoster is implicated in half of the cases.

PATHOPHYSIOLOGY OF ISCHAEMIC STROKE SUBTYPES

Cerebral infarction is not a single disease and the differentiation of several clinical, pathophysiologic and etiologic subtypes may be critical for adequate management of patients.

The most common mechanisms of ischaemic stroke is embolic, either from an atheromatous arterial lesion (artery to artery thromboembolism) or from the heart (cardio embolism). Less commonly, in situ occlusion of an extra cranial or a cerebral artery may be incriminated in the absence of embolism.

- First, when the occluded artery is a small perforating branch without collateral supply i.e. (lacunar infarct).[29]

- Second, when large-artery occlusion may produceHaemodynamic failure in the corresponding territory

  because of lack of functioning anastomoses (Haemodynamic infarction).

-

- Finally abnormalities of the blood itself may lead to ischaemic stroke (eg) coagulation disorders hyper viscosity, anemia leukemia and related disorder.

Intracranial atherosclerosis play a major role in Asians and to a lesser extent in blacks. In whites, extra cranial atherosclerosis causes artery to artery embolism. However this distinction is valid mainly for anterior circulation. While recent studies have shown that intracranial vertebral artery or basilar artery atherosclerosis is also an important cause of posterior circulation infarcts.[30]

MIDDLE CEREBRAL ARTERY – SUPERFICIAL TERRITORY INFARCTS

Superficial branches of the middle cerebral artery (MCA) originate distal to the origin of lenticulostriate arteries. As they course in the subarachnoid space, they are called pial branches. They supply the cortical, sub cortical territory of the MCA after the MCA trunk divide in to two (upper and lower) or three (upper, middle and lower) divisions which in their turn divide into several branches.

MCA pial territory infarcts may be partial when only a distal branch is occluded, or they may be rather large when the occlusion is more proximal at the level of the MCA bifurcation or trifurcation and the

Collateral system is not adequate. Because one characteristic of the pial artery network is to have extensive anastomoses, multiple distal emboli are necessary.

Actually at least, half of the patients with MCA pial territory infarct may show angiographic evidence for distal occlusion, suggesting embolism and most of the angiographically normal cases may be due to delayed performance of angiography because these occlusions tend to disappear early.

The presumed cause of embolism is large-artery disease (>50%)
Internal carotid artery (ICA) or MCA stenosis or occlusion in one third of the patients and cardiac disease in one quarter of the patients.[31] Interestingly, potential cardiac sources of embolism are particularly common with infarcts in the territory of the lower division of the MCA, which are also associated with more disability than infarcts in the territory of the upper division.

FRESH ISCHAEMIC INFARCT

Because most of the frontal, temporal and parietal lobes are supplied by the MCA pial branches, the Neurologic picture may be variable according to the location of the infarct.

INFARCTS IN THE TERRITORY OF THE DEEP PERFORATORS FROM THE CAROTID SYSTEM

In contrast to the pial artery network, the deep perforators from the distal ICA or the MCA trunk are terminal branches that perforate the basal part of the cerebral hemispheres. For that reason, occlusion of one orseveral perforators is always associated with an infarcts usually small in the corresponding territory. These small deep infarcts are often called '***Lacunar, `but it should be remembered that lacunar may be caused by non*** ischaemic processes such as small haemorrhage or nor ischaemic dilatation of periarteriolar space.

It is widely accepted that lacunar infarcts are usually due to in situ occlusion of the corresponding small perforator by a micro atheromatous or lipohyalinotic process associated with chronic arterial hypertension. This assumption appears correct for very small lacunar infarcts(<0.3-0.5cm) associated with occlusion of one single perforator but these infarcts are usually asymptomatic.[29] Although small artery disease probably remains a leading etiology, in larger (0.5 -1.5 cm or larger) and symptomatic small deep infracts, other potential causes may also be considered, since more than one third of these patients may have a potential cardiac source of embolism or larger artery disease (>50%ICA stenosis or occlusion, often in the absence of concomitant hypertension.[32]

Embolism to the MCA trunk is a particularly common cause of complete lenticulostriate territory inaction (known as large striate capsular infracts or extended infracts of the lentiform nucleus), by occluding the lenticulostriate arteries at their origin while collateral circulation explains sparing of the superficial pial territory.[33]

While it is unclear if large-artery or cardiac disease is just co-incidental in many patients with small deep [infarcts, it is likely that atherosclerosis of the MCA trunks (or of the basilar artery for small paramedian infarcts in the brain stem), which can occlude the origin of deep perforators has largely been overlooked as a potential etiology of small deep infarcts.[34] Moreover, hypertension does not seem to be the only factor associated with small-artery disease leading to lacunar infarction, Diabetes mellitus should also be considered.

Clinical manifestations are largely dependent on the size of infarct. The larger infarcts may produce dysfunction not markedly different from superficial MCA territory infarcts. Smaller infarcts have often been linked to isolated contra lateral motor or sensory disturbances (lacunar syndromes).

THE CLASSIC LACUNAR SYNDROMES ARE:

1. Pure motor Hemiparesis from an infarct in the posterior limb of the internal capsule or basis pontis, the face, arm and leg are almost always involved.
2. Pure sensory stroke-from an infarct in the ventro lateral thalamus.
3. Ataxic Hemiparesis –from an infarct in the base of the pontis.
4. Dysarthria and a clumsy hand or arm due to infarction in the base of the pons or in the genu of the internal capsule.
5.
6. Pure motor Hemiparesis with motor or Brocas aphasia due to Thrombotic occlusion of a lenticulostriate branch supplying the genu and anterior limb of the internal capsule and adjacent white matter of the corona radiata.

The artery of Heubner from the anterior cerebral artery (ACA) and the anterior choroidal artery from the carotid siphon are not only perforators, because they also supply cortical territories. Thus, their system of supply can be compared with that of the MCA and their etiologic spectrum of infarction is similar.[35]

ANTERIOR CEREBRAL ARTERY

Although the ACA originated from the carotid system at the same level as the MCA, ACA territory infarcts are between 20-30 times less common than MCA territory infarcts. However, Etiologic patterns do not differ between MCA and ACA territory infarcts.
Infarcts in the territory of Heubner's artery or in the territory of the anterior striate branches are usually discussed together with lenticulostriate infarcts in general.

In ACA, pial territory infarcts, the association of crural Hemiparesis, mutism at onset, transcortical motor aphasia, frontal tasks impairment, mood disturbance, incontinence, grasp reflex and unilateral left apraxia may help to localize the infarct before Computed Tomography or Magnetic Resonance Imaging, but proportional (arm-leg-arm) hemisparesis or hemisensory defect, hemineglect or confusional state may be misleading. Simultaneous bilateral ACA territory infarction may occur in relation to a common origin of both ACAs. Akinetic mutism with incontinence and bilateral grasp reflex is suggestive of this type of infarct, which is uncommon (<10%)

BORDER ZONE CEREBRAL INFARCTS

Infarction may develop at the level of the collateral border zone between two main pial arterial territories. Those extra territorial infarcts are commonly called watershed or distal field infarcts. They usually occur between the ACA and MCA territories anterior water shed infarcts or between the MCA and posterior cerebral artery (PCA) territories – posterior water shed infarcts.

In anterior water shed infarcts, hemisparesis, predominating in the lower limb, with transcortical motor aphasia when lesion is on the left, is the most common Neurologic finding when the infarct predominates in the subcortical white matter, mimicking ACA territory infarction. However, when the infarct is limited to the cortex, proximal brachial hemisparesis is present because junction of the ACA and MCA territories is at the level of the arm-shoulder representation on the motor strip, thus in bilateral anterior watershed cortical infarcts, a picture bi-brachial paralysis (man-in –the-barrel)may occur.

Posterior watershed infarcts yield a Neurologic picture that is similar to that of posterior MCA pial territory infarcts except for a more common occurrence of transcortical sensory aphasia.

Bilateral watershed infarcts often have a symmetrical pattern. They usually develop in relation to episodes of severe hypotension, cardio circulatory distress, prolonged hypoxemia or bilateral severe carotid disease.[36] Ventero lateral watershed infarcts are also associated with some degree of haemodynamic failure (hypotension, bradycardia, high

hematocrit level) in patients with ipsilateral carotid occlusion or tight stenosis. They are good examples of haemodynamic infarcts, though microemboli may account for some border zone infarcts.

An infarction between the deep and superficial (pial) territories of the MCA is uncommon. It is sometimes called a sun cortical watershed or internal watershed infarct.[37] However the term watershed may be inappropriate because it implies a border zone between two pial territories at the level of their collateral network. Infact no such collaterals exist between and the pial branches of the MCA system. For this season, the term subcortical junctional or border zone infarcts seems more appropriate [38] Hemisparesis with or without hemisensory disturbance is the most common Neurologic disturbance.

POSTERIOR CEREBRAL ARTERY SUPERFICIAL TERRITORY INFARCTS

The superficial (pial) branches of the PCA include the hippocampal, medial temporo –occipital, splenial, and internal occipital and calcarine branches. The posterior choroidal branches have an internal temporal pial network, but they are usually considered with the deep branches of the thalamus. Infarcts limited to the territory of just one branch of the PCA are the most commonest type of PCA pial territory infarction(uniterritorial), often involving the calcarine artery territory. Isolated mediotemporal involvement is rare. The most common biterritorial infarct combines calcarine and internal occipital arteries territory involvement.

The Neurologic manifestations are dominated by visual symptoms, which may be simple (hemianopia) or complex (alexia, achromatopsia, agnosia, visual memory impairment).

In pathologic series, PCA infraction is often due to compression by edema during temporal lobe herniation. In a clinical setting the etiology is usually embolic, mainly from the heart, vertebro basilar atherosclerosis.

THALAMIC INFARCTS

The arterial supply to thalamus may be divided into four main groups.

1. The Paramedian or thalomo perforate branches from the P1 segment of the PCA. They also supply the most rostal Paramedian part of the mid brain (vertical gaze dysfunction, disturbed consciousness, amnesia and other neuro behavioural dysfunction).
2. The infero lateral or thalamo geniculate branches from the P2 segment of the PCA. These arteries supply the ventero lateral mass of the thalamus (hemisensory disturbances, hemi ataxia).
3. The posterior choroidal arteries (one lateral and one medial group) from the P2 segment of PCA. These supply posterior part of thalamus and also contribute to supply of the geniculate bodies and medial temporal lobe together with the anterior choroidal artery (mainly visual hemifield disturbances such as horizontal sectoranopia).
4. The tubero thalamic or polar branches originate from posterior communicating artery so that they are laterally at the interfall between the carotid and vertebro basilar systems. They supply the anterolateral part of the thalamus (Neuropsychologic dysfunction such as dysphasia, amnesia, neglect).

The etiology of thalamic infarct is varied. Small vessel disease associated with hypertension or diabetes accounts for not more than one third of the cases, while cardio

embolism and artery –to-artery embolism accounts for atleast 25% to 30%. Other causes such as arteritis, migraine and so on may also be responsible. Usually simultaneous occlusion of several perforators (from embolism) may be necessary to lead to infarct.

BRAIN STEM INFARCTS

Mid brain, pontine and medullary infarcts usually develop in characteristic territories in relation to a stereotyped blood supply system which includes (from medial to lateral side) Paramedian perforating branches and short circumferential arteries directly from the basilar artery and large circumferential arteries, which are infact the three cerebellar arteries:

1. The Superior Cerebellar Artery (SCA)
2. Anterior Inferior Cerebellar Artery (AICA) and
3. Posterior Inferior Cerebellar Artery (PICA) and supply the dorsal brain stem as well as their cerebellar territory.Most of the clinically relevant brain stem infracts involve the paramedian and lateral (short circumferential branches) territories. Thus, they may be associated with small-vessel disease (lacunar infraction) but also with basilar artery (for the pons and mid brain) or vertebral artery (for the medulla) disease that obstructs the mouth of these small arteries (branch disease). Large embolism, which may stop more proximally in the basilar artery, lead to large infracts not limited to the brain stem. The Neurologic manipulations caused by brain stem infracts are multiple.

CEREBELLAR INFRACTS

1. **PICA Territory Infracts** PICA territory infracts are the most common type of symptomatic cerebellar infarcts. Most cases seem related to atheromatous occlusion of the vertebral artery, less commonly the PICA itself.

2. **AICA Territory Infracts**

AICA territory infarcts are the less common type of cerebellar infarcts. Infarcts in the lateral part of the lower pons is usual in association with cerebellar involvement.[39] Contrary to PICA and SCA territory infarcts, cardio embolism seems to be an uncommon cause. Atherosclerosis plays a major role.

3. **SCA Territory Infarcts**

In SCA territory infarcts, clinically relevant brain stem (mid brain) involvement is less common than in AICA territory infarcts, where cardio embolism is a classic cause.

OTHER CEREBELLAR INFARCT

Large cerebellar infarcts are usually MCA territory infarcts in patients with AICA aplasia. They are typically responsible for a rapid deterioration, tonsillar herniation and death in the absence of surgical intervention.

Watershed cerebellar infarcts may occur at the border zone between PICA, SCA and AICA territories. Their clinical diagnosis is controversial since the overlap of the cerebellar arteries may be particularly variable. Small cerebellar infarcts have been reported in presumed cerebellar border zones, but also within the main cerebellar territories.

Venous cerebellar infarcts are usually large with a pseudo tumoural course.

INVESTIGATIONSCOMPUTED TOMOGRAPHY (CT)

The role of Computed Tomography in the diagnosis of cerebral infarction is well established. CT scan distinguish between an ischaemic bland – non haemorrhagic stroke, haemorrhagic infarction and primary intracerebral Haemorrhage.[41]

In the clinical setting of a transient ischaemic attacks (TIA) the CT scan is usually normal, however the detection of white matter or capsular hypodensity (chronic ischaemic change) establishes the presence of underlying vascular disease.

The classic neuropathologic process that occurs during the evolution of an infarction is well reflected by the CT scan. The radiologic imaging characteristics are divided in to four stages and are dependent on the time from the onset of ictus. These stages are divided into

1. Hyperacute — less than 24 hrs
2. Acute — 24 hrs – 7 days.
3. Subacute — 8 – 21 days
4. Chronic — more than 21 days.

SUPERFICIAL MIDDLE CEREBRAL ARTERY INFARCT

MAGNETIC RESONANCE IMAGING (MRI)

Image contrast with magnetic resonance imaging is dependent on three tissue variables. T1 – relaxation, . T2 – relaxation time and proton density.

Ischaemia one hour after the event can be detected by MR imaging. MRI reliably documents the extent and location of the infarction an all area of the brain, including the posterior fossa and cortical surface. Diffusion weighed imaging is more sensitive for early brain infarction. Magnetic Resonance angiography is highly sensitive for extra cranial internal carotid plague as well as intracranial stenosis of large vessels. MRI proves superior information compared with CT in nearly every case of stroke.

CEREBRAL ANGIOGRAPHY

Conventional X-ray cerebral angiography is the “gold standard” for identifying and quantifying atherosclerotic stenosis of the cerebral arteries and other pathologies. Recent studies have documented that intra arterial delivery of thrombolytic agents to patients with acute MCA infarct can effectively recanalize vessels and improve clinical outcomes.

BASELINE TESTS FOR MOST ISCHAEMIC STROKE PATIENTS.

SI No.	Investigation	Treatable disorders detected
1.	Full Blood Count	Anaemia, polycythaemic, Leukemia, Thrombocytopenia.
2.	ESR	Vasculitis, Infective endocarditis hyperviscosity
3.	Plasma glucose	Diabetes, Hypoglycemia
4.	Plasma cholesterol	Hyper cholesterolemia
5.	Syphilis serology	Syphilis, Anti cardiolipin antibody
6.	Urine analysis	Diabetes, Renal disease.
7.	Electro Cardiogram	LVH, arrhythmias, conduction block, myocardial ischaemia or infarction.

PREDICTION OF STROKE OUTCOME

The outcome of stroke is influenced by many factors. Among them, some of the most important are demographic factors such as age, sex, etc, risk factors, clinical examination findings, laboratory tests and imaging. These factors provide important insight regarding outcome.

1.

2. **DEMOGRAPHIC FACTORS**

a. **Age**

It is one of the major factors which can negatively influence the outcome. Poor outcome in old age is due to increased frequency of secondary complications such as pneumonia, bed sores etc.

b. **Gender**

Stroke in males poses poor outcome. Endogenous estrogens in females are found to be neuroprotective and have flow preserving effects.

3. **RISK FACTORS**

Previous stroke and atrial fibrillation causes more disability and associated with increased mortality.

4. **CLINICAL FINDINGS**

a. Level of Consciousness and Gaze Deviation

A decrease in the level of consciousness and presence of gaze deviation indicates poor outcome.

b. Blood Pressure

Systemic hypotension can cause a fall in cerebral blood flow which may cause a decreased blood flow to the infracted area.

A rise in BP may have long term adverse effects on the blood brain barrier. Under severe hypertension the infracted area can go for haemorrhagic transformation.

Temperature

A two fold increase in the relative risk for poor outcome in stroke is seen with every 1^{o}C rise of temperature. This effect may be due to excitotoxic neurotransmitters.

COMPLICATIONS

The most important local complication of cerebral infarction is the development of cerebral oedema, which impairs, possibly only temporarily, local blood flow and neuronal function over a wider area than just the infarct and, if extensive, causes transtentorial herniation. There are a number of general complications of acute paralysis which include bronchopneumonia, particularly if consciousness or swallowing are impaired; venous thromboembolism; pressure sores and septicemia; urinary infection, particularly if catheterization is necessary, and eventually uraemia; contractures in spastic limbs; frozen shoulder; cardiac rhythm disturbances; and mood disorder(Table). Death in the first week is almost always due to the infarct itself and the effects of cerebral oedema, but later it is more often due to one of the general complications, particularly pneumonia.

GENERAL COMPLICATIONS OF STROKE

Respiratory

Pneumonia

Inhalation

Pulmonary embolism

Cardiovascular

Myocardial infarction

Cardiac failure

Cardiac arrhythmia

Neurogenic pulmonary oedema

Infections

Pneumonia

Urinary

Skin

Septicemia

Metabolic
Vomiting
Dehydration
Electrolyte imbalance
Hyperglycemia
Renal failure
Mechanical
Spasticity
Contractures
Malalignment/subluxation/frozen shoulder
Falls and fractures
Osteoporosis
Ankle swelling
Peripheral nerve pressure palsies
Others
Pressure sores
Depression, anxiety, apathy
Epileptic seizures
Deep venous thrombosis
Acute gastric ulceration, Incontinence of urine/faeces

COURSE AND PROGNOSIS

When the patient is seen early in the course of cerebral thrombosis, it is difficult to give an accurate prognosis. No rules have yet been formulated that allow one to predict the course with confidence. A mild paralysis today may become a disastrous hemiplegia tomorrow, or the patients condition may worsen only temporarily for a day or two. In basilar artery occlusion, dizziness and dysphagia may progress in a few days to total paralysis and deep coma.

The course of cerebral thrombosis is so often progressive that a cautions attitude on the part of the physician is justified in what first appears to be a mild stroke.

As indicated above, progression of the stroke is due most often to increasing stenosis of the involved artery by mural thrombus. In some instances, extension of the thrombus along the vessel may block side branches and hinder anastomotic flow. In the basilar artery, thrombus may gradually build up along its entire length. In the carotid system, Thrombus at times propagates distally from the site of origin in the neck to the supraclinoid portion and possibly into the anterior cerebral artery, preventing collateral flow from the opposite side.

In middle cerebral occlusion, retrograde thrombosis may extend to the mouth of the anterior cerebral, perhaps secondarily infracting the territory of the vessel. Embolic particles from the site of an incompletely thrombosed artery (artery –to- artery embolism) may precipitate an abrupt change. Sometimes a completely thrombosed artery or an artery whose lumen is narrowed by a dissecting aneurysm can be the source of an embolus to more distal branches after a period of several days.

Several other circumstances influence the immediate prognosis in cerebral thrombosis. In the case of very large infarcts, swelling of the infracted tissue may occur, followed by displacement of central structures, tentorial herniation, and each of the patients after several days. Smaller infracts of the inferior surface of the cerebellum may cause a fatal foramen magnum herniation. Mider degrees of swelling and increased intracranial pressure may cause apparent progression for 2 or 3 days but do not prove fatel. In extensive basilar infraction associated with deep coma, the mortality rate approaches 40 percent. If coma or stupor is present from the beginning, survival is largely determined by the success in keeping the airway clear,

controlling brain edema, preventing aspiration pneumonia, and maintaining fluid and electrolyte balance. Respiratory and urinary infections are constant dangers; once they begin, there is usually a rapid decline in the patient s condition as body temperature rises. With smaller Thrombotic infarcts, the mortality is 3 to 6 percent.

Characteristically, the paralyzed muscles are flaced in the first days or weeks following a stroke; the tendon reflexes are usually unchanged but may be slightly increased or decreased. Gradually Spasticity develops, and the tendon reflexes become brisker. The arm tends to assume a flexed adducted posture and the leg an extended one. Function is rarely if ever restored after the slow evolution of Spasticity. Conversely, the early development of Spasticity in the arm or the early appearance of a grasp reflex may presage a favorable outcome. In some patients with extensive temporoparietal lesions, the hemiplegia remains flaccid. If the internal capsule is not interrupted completely in a stroke that involves the lenticular nucleus or thalamus, the paralysis may give way to hemichoreoathetosis, hemitremor, or hemi ataxia, depending upon the particular anatomy of the lesion. Bowel and bladder control usually returns; sphincter disorders persist in only a few cases. Often the hemiplegic limbs are at first tender and ache on manipulation. Nevertheless, physiotherapy should be initiated early in order to prevent paeudocontracture of muscles and periarthritis at the shoulder, elbow, wrist, knuckles, knee and ankle. These are frequent complications and often and source of pain and added disability, particularly in relation to the shoulder. Occasionally, atrophy of bone and pain in the hand may accompany the shoulder pain (shoulder – hand syndrome). An annoying feeling of dizziness and unsteadiness often persists after damage to the vestibular system in brainstem infarcts.

Recurrent convulsive (epileptic) seizures are relatively uncommon sequelae of Thrombotic strokes in comparison to embolic cortical infarcts, which are followed by recurrent focal or generalized seizures in more than 20 percent of patients.

Many patients complain of fatigability and are depressed, possibly more so after strokes that involves the left frontal lope (Stark stein et al.). The explanation of these symptoms is uncertain; some are expressions of a reactive depression. Only a few patients develop serious behaviour problems or are psychotic after a stroke, but paranoid trends, ill temper, stubbornness, and peevishness are common.

Finally, in regard to prognosis, it must be mentioned that having had one Thrombotic stroke, the patient is at risk in the ensuing months and years of having a stroke at the same or another site, especially if there is hypertension or diabetes mellitus. When multiple infarcts occur over a period of months or years, a dementia may develop, in addition to

focal cerebral deficits. As a group these cases are referred to as multi-infarct dementia. In some of these cases, the major lesions involve the white matter with relative sparing of the cortex and basal ganglia. This type of lesion is often referred to as a Binswanger`s subcortical encephalopathy, which is equated with multiple white matter infarcts and lacunas. The part of the white matter that is destroyed has been shown to lie in the border zones between the penetrating cortical and basal ganglionic arteries.

TREATMENT

There is little that medical treatment and nothing that vascular surgery can do to later the immediate outcome after cerebral infarction. In theory the reduction of cerebral oedema by Mannitol, glycerol, or dexamethasone should be useful, but there have been no adequate

clinical trails. Thrombolysis causes intracerebral haemorrhage and this risk may not be outweighed by the potential benefit, if any. Aspirin is currently being evaluated. Heparin has been recommended for stroke-in-evolution, although there have been no convincing trials and, since some cases may be due to haemorrhage into infracted brain or even to primary intracerebral haemorrhage from the beginning, this treatment is not normally to be recommended. It is important to remember that there are many other reasons for stroke patients to deteriorate, and some are potentially reversible.

CAUSES OF NEUROLOGICAL DETERIORATION AFTER STROKE

Local	Extension of thrombus
	Recurrent embolism
	Recurrent haemorrhage
	Haemorrhagic transformation of the infarct
	Cerebral oedema
	Brain shift and herniation
	Hydrocephalus
	Epileptic seizures
General	Hypoxia (pneumonia, pulmonary embolism, cardiac failure
	Hypotension (cardiac failure, cardial arrhythmia, septicaemia,
	Pulmonary embolism, dehydration, pneumonia, drugs,
	bleeding or perforated peptic ulcer)
	Infection (chest, urine, septicaemias)
	Dehydration
	Hyper-or hypoglycemia
	Sedatives/hypnotics,Depression

The complications of cerebral infarction are often preventable and treatable. Chest physiotherapy and care of the airway, particularly in unconscious patients and those with difficulty in swallowing, will reduce the risk of

pneumonia which, if it occurs, can be treated with antibiotics. Occasionally intubation and tracheostomy are needed in patients who cannot protect their airway due to impaired brain-stem reflexes, but who are otherwise expected to have a reasonable good prognosis. Nasogastric tube feeding is used for adequate hydration and electrolyte balance in patients who cannot swallow, and later for feeding if necessary. Good nursing should prevent pressure sores. Early physiotherapy will reduce the risk of contractures, pain, and stiffness in hemiplegic limbs and leads naturally on to active physical rehabilitation. Urinary catheterization is often avoidable in males for whom an appliance is a better alternative but in females it may be necessary so that the skin can be kept dry to reduce the chance of pressure sores. Cardiac arrhythmias should be treated on their merits but are not normally a problem. Since cerebral infarcts can become haemorrhagic, it is uncertain whether deep venous thrombosis in the legs and pulmonary embolism should be prevented, or even treated, with antithrombotic drugs, but the benefit of high-dose heparin followed by oral anticoagulation for major pulmonary embolism probably outweighs the risks. Epilepsy, if it occurs, should be treated in the normal way

MATERIALS AND METHODS

Setting	**:**	Medical wards P.S.G Hospital
Study	**:**	Single centre observational Prospective hospital based study.
Period of Study	**:**	August 2009 October 2009

All stroke patients admitted within the above period and who satisfied the set criteria were included.

INCLUSION CRITERIA

1. **Patients with stroke as defined by WHO criteria**

   Rapidly developing clinical signs of focal or global (coma) neurological deficit lasting more than 24 hrs or leading to death with no apparent cause other than vascular origin.

2. All patients who presented within 48 hours of onset of stroke and who gave informed consent to participate in the study were included.

EXCLUSION CRITERIA

1. Patients with sub arachnoid haemorrhage, extradur Haemorrhage, subdural haemorrhage and intra cerebral haemorrhage were excluded by CT.
2. Patients with previous history or TIA/RIND were excluded.
3. Patients with gout were excluded
4. Patients who were alcoholics were excluded.
5. Patients taking drugs causing hyperuricaemia were excluded from the study(eg) drugs like:

   Loop diuretics

   Anticancer drugs (Cisplatin, cyclosporine,

   Cyclophosphamide)

   ATT (Pyrazinamide, Ethambutol)

   Aspirin, Pentamidine, Theophylline, Ketoconazole

   Levodopa, isotretinoin.

   Patients with previous history of coronary vascular events were excluded.

Diagnostic procedures treatment and all stages of rehabilitation took place according to prevailing norms and protocols. The treating physician's advice was exercised if and when found necessary.Serum uric acid was measured when the patient was admitted and was correlated with functional recovery of the patients after 4 weeks patients were reviewed 4 weeks after onset of stroke and were stratified using Glasgow Outcome Scale(GOS).

GOS was used to asses the functional outcome and residual neurological deficits.

GLASGOW OUTCOME SCALE

1. Indicates death
2. **Vegetative state** (patients is unable to interact with environment)
3. **Severe disability** (patient is unable to live independently but can follow commands)
4. **Moderate disability** (Patients is capable of living independently but unable to return to work or school).
5. **Mild or No disability** (Patient can return to work or school).

Scale 4 x 5 - Favourable outcome

Scale 1, 2 & 3 - Unfavourable outcome

LABORATORY ASSESSMENT OF URIC ACID (URICASE METHOD)

A reagent kit is available at the central biochemistry laboratory, GGH. This reagent kit is for quantitative estimation of uric acid in serum or plasma.

Principle

Uric acid + O_2 - $2H_2O$ Uricase Allantoin + CO_2 + H_2O_2

$2H_2O_2$ + 4 Amino antipyrine + DHBS

----------Chromogen + $4H_2O$

Uric acid in serum is oxidised by uricase to allantion and hydrogen peroxide. Hydrogen peroxide thus generated is acted upon by peroxidase and oxidizes the chromogen (4 amino antipyrine + DHBS) to a red coloured compound which is read at 520 nm

(490-550 nm) or with a green filter. The colour intensity at 520nm is proportional to the concentration of the uric acid in the sample.

The reagent kit is provided with three solutions namely

1. Uric acid (enzyme, chromogen)
2. Uric acid (buffer)
3. Uric acid (standard 5mg/dl)

This reagent is for invitro diagnostic use.

PREPARATION OF WORKING SOLUTION

A working solution is prepared by dissolving the content of vial labeled 1, uric acid (enzyme) with the quantity of 2. Uric acid (buffer). The two solutions are mixed gently.

Specimen Collections

Fresh clear serum with no hemolysis is the specimen of choice.

However plasma collected from blood with heparin as an anti coagulant may be used.

Procedure

The sample and working solution should be brought to room temperature prior to use.

25µ1 of the sample is mixed with 1 ml of working reagent. The solution is incubated at 37^{o}C for 5min or 10 min at room temperature. The wavelength of the solution and that of the blank reagent solutions are compared at 520 nm or with green filter.

ANOTHER PROCEDURES FOR 2.5 ML CURETTE CAPACITY IS

	Blank	Standard	Test
Working reagent	2.5 ml	2.5 ml	2.5ml
Standard	-	0.05ml	-
Sample	-	-	0.05ml

Mix and incubate for 5 min at 37 ° C and read absorbance of the best and standard against reagent blank at 520 nm or with green filter.

Calculations

$$\text{Uric acid concentration mg/dl} = \frac{\text{Absorbance of test}}{\text{Absorbance of Standard}} \times 5$$

To convert uric acid concentration from mg/dl to μmoles/L, the following equation is used

μmoles/L = 59.5 x mg/dl

mmoles/L = 0.0595 x mg/dl

Normal serum uric acid level is 3.2 – 6.0 mg/dl.

In our present study, uric acid was determined within 48 hours after the onset of stroke. Ischaemic stroke was confirmed by CT scan 51 patients who fulfilled the criteria were taken under study. None of the patients underwent Thrombolysis. They were treated with antiedema, anti-platelet drugs and physiotherapy. Outcome noted by Glasgow outcome scale.

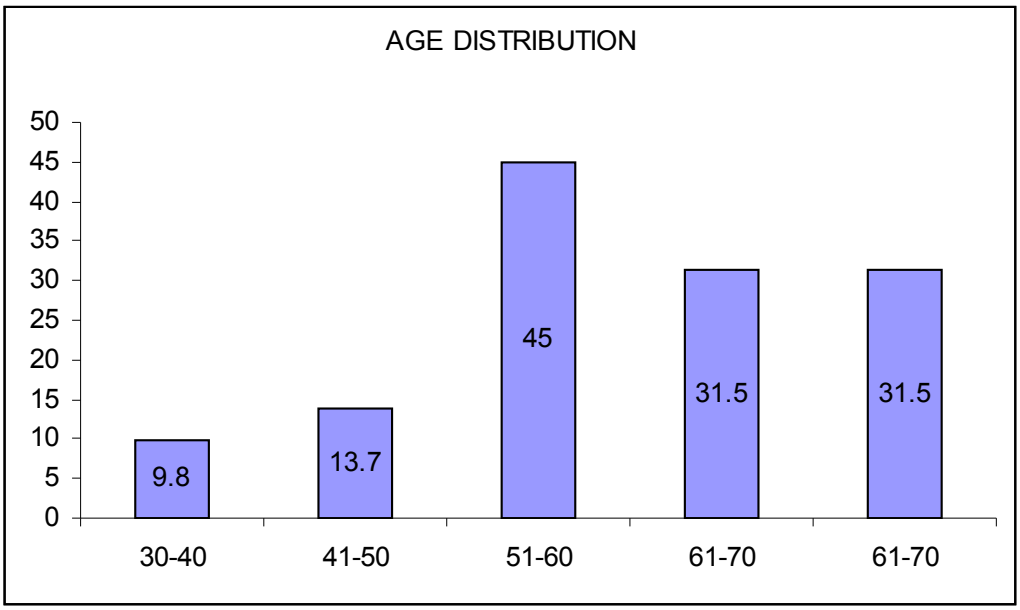
OBSERVATION AND RESULTS

AGE DISTRIBUTION

Age of the 51 selected patients ranged from 30-70 years.

Age	Males	Females	Total	Percentage
30-40	5	0	5	9.8
41-50	6	1	7	13.7
51-60	12	11	23	45.0
61-70	10	6	16	31.5
61-70	10	6	16	31.5
Total	**33**	**18**	**51**	**100%**

Out of 51 patients, 5 belonged to the age group of 30-40 years. Most of the patients were in the age group of 51-60 years. They constitute about 45% of the patients totally studied.

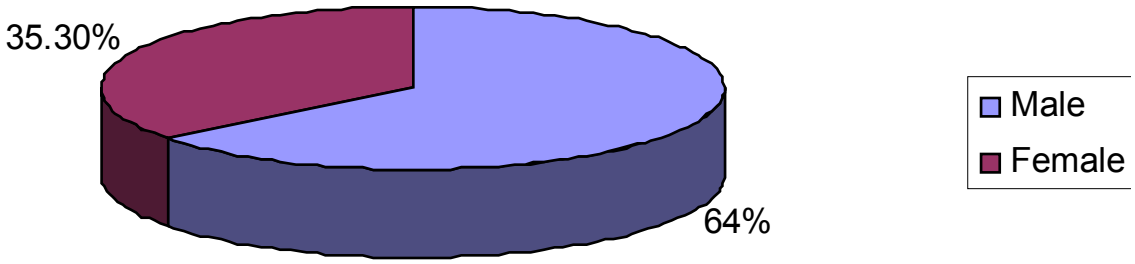


Age in Years

SEX DISTRIBUTION

	No. of patients	Percent
Male	33	64%
Female	18	35.3%
Total	**51**	**100%**

Out of 51 patients, 33 were males and 18 females.

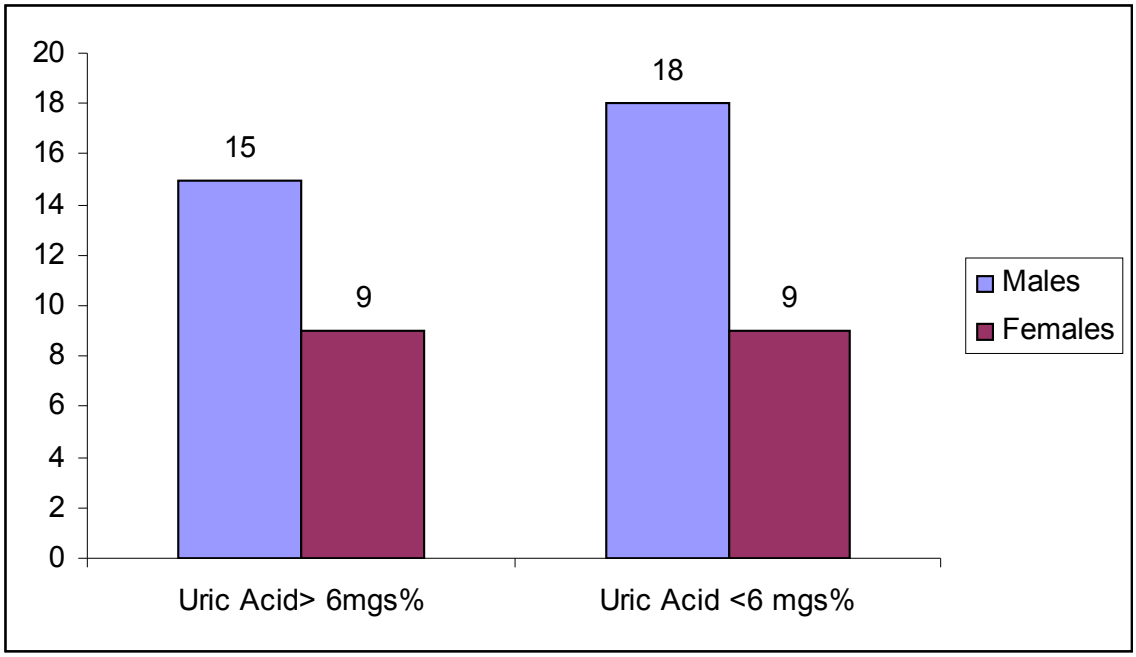


SEX DISTRIBUTION

	Uric Acid> 6mgs%	**Uric Acid <6 mgs%**	**Total**
Males	15	18	33(64.7%)
Females	9	9	18(35.3%)

45% of the males and 50% of females showed raised serum uric acid levels.

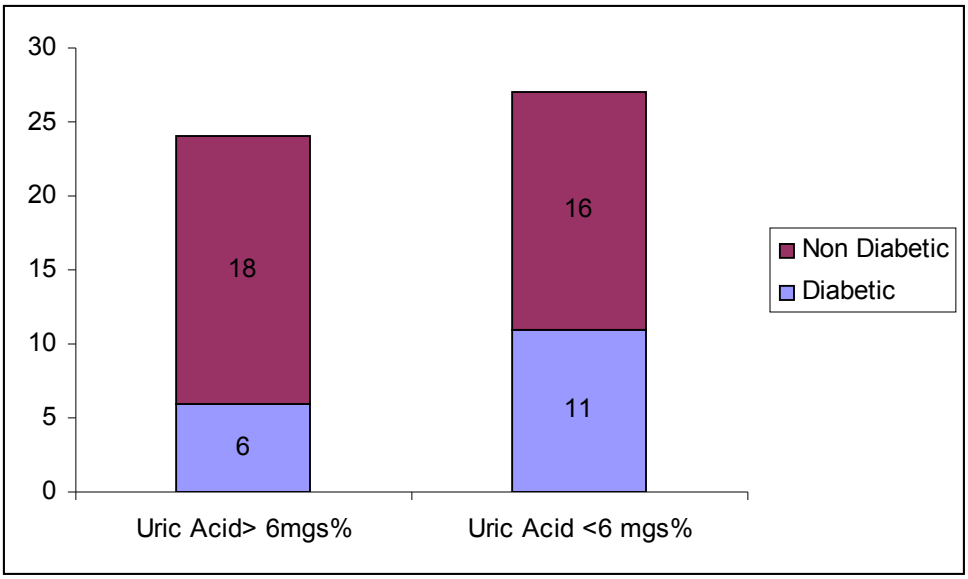
DIABETIC AND URIC ACID



DIABETIC AND URIC ACID

	Uric Acid> 6mgs %	**Uric Acid <6 mgs%**	**Total**
Diabetic	6	11	17(33.3)
Non Diabetic	18	16	34(66.7)
Total	**24(7)**	**27(53)**	**51(100)**

17 out of 51 patients were diabetic (ie. 33.3%). Among them 6 had serum uric acid > 6 mg% (ie.35.2%). Among non diabetics 18 out of 34 patients were found to have elevated serum uric acid >6 mg% (ie.)60%.



STROKE PATIENTS

DIABETES AND OUTCOME

Diabetes

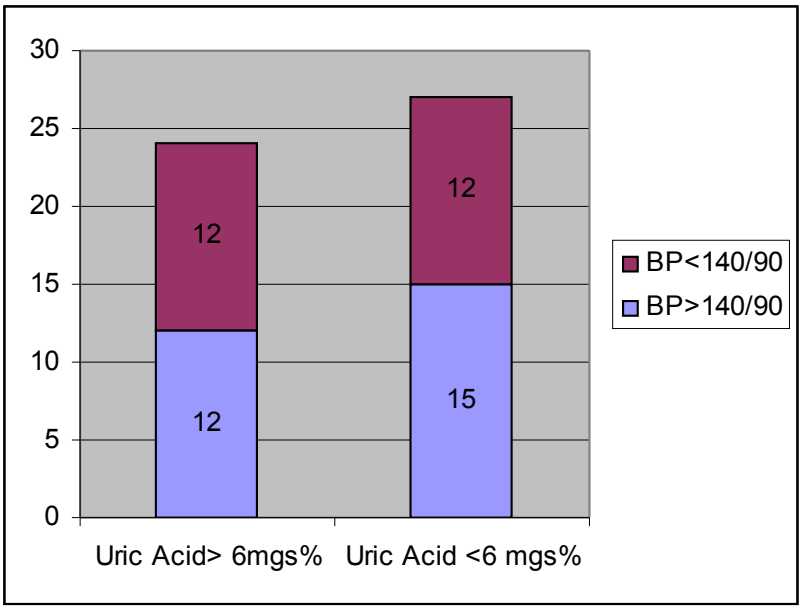
Good Outcome	Poor Outcome
8	9

9 out of 17 diabetic patients had poor outcome ie 53

HYPERTENSION AND URIC ACID

	Uric Acid> 6mgs %	Uric Acid <6 mgs %	
BP>140/90	12	15	27(53)
BP<140/90	12	12	24(47)
Total	24	27	51

53% of the patients were hypertensive and among them 44% were found to have uric acid levels greater than 6mgs%.

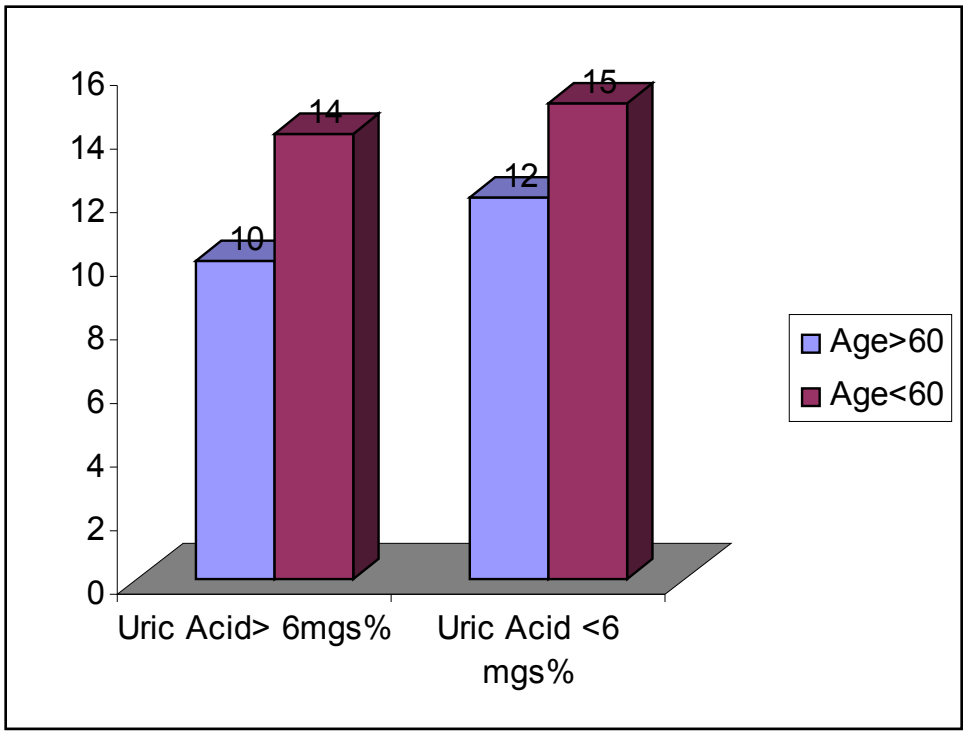


HYPERTENSION AND URIC ACID

AGE AND URIC ACID

	Uric Acid> 6mgs %	**Uric Acid <6 mgs %**	**Total**
Age>60	10	12	22(43)
Age<60	14	15	29(57)
			51

Out of 51 patients, patients with age of 60 years and above were 22 i.e.,43% Among them, 10 have elevated uric acid levels.

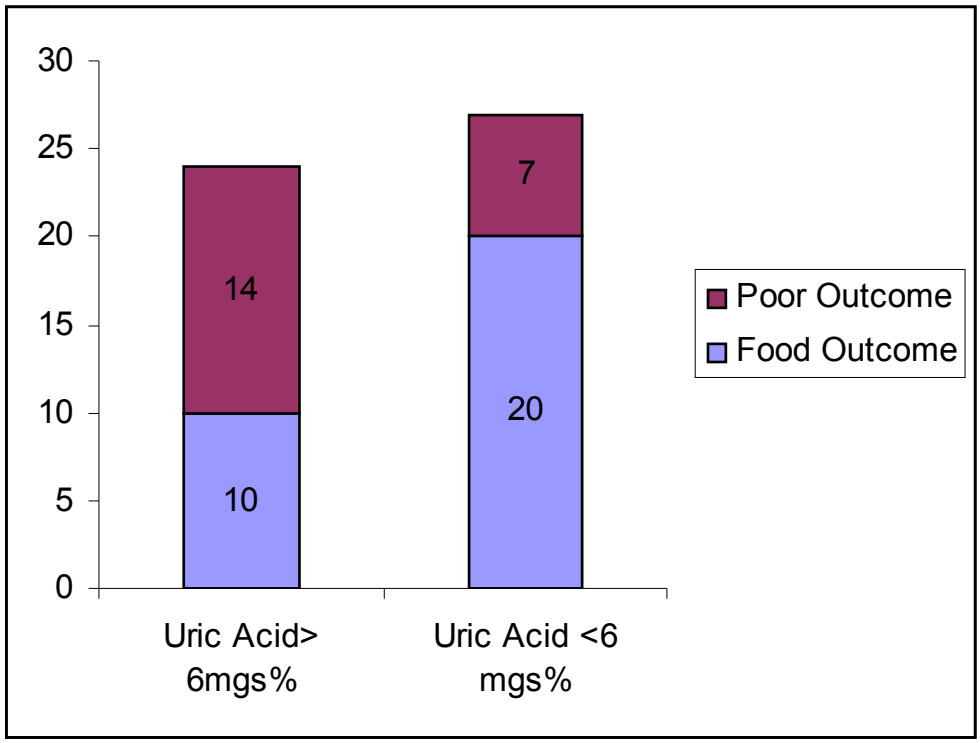


AGE AND URIC ACID

URIC ACID AND OUTCOME

	Uric Acid> 6mgs %	**Uric Acid <6 mgs %**	
Food Outcome	10	20	30(59%)
Poor Outcome	14	7	21(41%)
	24	7	51

30 out of 51 patients had good outcome, with elevated uric acid levels found 10 among them



URIC ACID AND OUTCOME

DISCUSSION

Uric acid which is an end product of purine metabolism has long been considered only in the pathogenesis of gout and uric acid stones. Its anti-oxidant functions and its various role in the pathogenesis of hypertension, cardiovascular and cerebro vascular events are considered now only. Various studies conducted during recent years on serum uric acid levels in vascular events have proven its prognostic significance.

Uric acid is also been considered as a marker for atherosclerosis. But the exact pathogenesis and whether it is the cause or effect of atherosclerosis remains to be elucidated.

AGE GROUP

In our study, most of the patients were in the age group of 50 years and above i.e., 76% of patients.

Stroke occurs predominantly in the middle and late years of life[42].

Age group of the patients has been found to have no correlation with serum uric acid levels in our study as per the statistical analysis by chi-square test. P value was not significant.

SEX DISTRIBUTION

64% of the patients were males in our study. Males show higher incidence of stroke as compared to females.

45% of males have raised serum uric acid levels more than 6 mgs% and 50 % of the female patients had raised uric acid levels.

In a study by Chamorro et al, stroke 2002 Apr;33(4), male sex showed raised serum uric acid levels. In our study most of the patients were males and a low number of females may falsely project them as patients with raised uric acid levels than males.

DIABETES

17 out of 51 patients had diabetes (33%) as diagnosed by Fasting Blood Sugar more than 125 mg%. 9 diabetic patients had a poor outcome (53%).

One of the bad prognostic factor in the outcome of stroke is the presence of associated diabetes mellitus. In our study 53% of diabetics had poor outcome.

The tests of significance didn't find any correlation between uric acid and diabetes. In a study by ***Lacto, Nishkanen and Ronnemaa et*** al**.,** serum uric acid levels was a strong predictor of stroke in Type II diabetes.

Since only 33% of patients were diabetic in our study this correlation may not be possible. We may need a large multicentred study.

HYPERTENSION

In our study 27 patients were hypertensive ie.53%. Among them 12 had raised serum uric acid levels i.e., 44% of the hypertensive patients.

The standard Chi-square test proved that there is definite association between hypertension and raised serum uric acid levels. P value is <0.05.

In a study by ***Wang JG and Stacssen et al.,*** there was a definite association between raised serum uric acid levels and isolated systolic hypertension.

In yet another study by ***Verdecchia P abd Schillaci et al.,*** it has also proved that there is a definite relation between serum uric acid and creatinine levels and essential hypertension.

Theodore R Fields et al., in his study of uric acid and cardiovascular disease – a possible pathogenic role discussed the `Chick and Egg' theory i.e. uric acid is whether the cause or effect of hypertension. In his study he include coronary artery disease also and found that uric acid has no etiological role to play in hypertension. His conclusion is that elevated uric acid is secondary to the systemic hypertension.

Iribarren, Folsom and Eckfeldt et al., tried to find the correlation between uric acid levels and asymptomatic carotid atherosclerosis. They found a positive correlation between the two and these can be used to predict the future cerebrovascular events.

Johnson, Keig and Feig et al., in their study of the pathogenic role of uric acid in hypertension and cardiovascular disease found a negative correlation. They conclude that uric acid has no pathogenic role in hypertension and cardiovascular diseases.

SMOKING

In our study, 22 patients were smokers (43%). Among those 22 patients, 9 had elevated uric acid levels.

By applying Chi-square test, P value was not significant, implicating no correlation between smoking and raised uric acid levels.

Angel ***Chamorro*** et al in his study has also proved that uric acid levels are independent of smoking. However associated atherosclerosis can elevate the uric acid levels falsely giving an impression that smoker having elevated uric acid levels.

URIC ACID IN THE PROGNOSIS OF STROKE PATIENTS

41% of the total patients under study group had poor outcome. Out of which 66% had raised serum uric acid levels.

The standard Chi square test was applied and it proved the statistical significance between poor outcome and raised uric acid levels.

According to ***Weir et al.,*** stroke 2003; serum urate can be an independent predicator of poor outcome and future vascular events after acute stroke.

In his study serum urate concentrations were measured in an unselected cohort of stroke survivors and were followed up. Urate was associated with a statistically significant three fold increase on relative risk of death, even after adjustment for other conventional risk factors.

In contrast, according to a study by Chamorro et al., stroke 2002, Apr. Serum uric acid elevation was associated with good prognosis in ischaemia stroke patients.

According to Chamorro et al., uric acid is a potent anti oxidant and hence it elevates as a compensatory mechanism in ischaemic tissues to protect the brain from free radical injury.

However it has been evident by experiments that uric acid is synthesized locally from infracted tissues, particularly during reperfusion. So its level in serum rises often in proportion to the size of the infarcted tissue, reperfusion status and the extent of the free radical injury.

CONCLUSION

In patients with acute ischaemic stroke:

- Serum uric acid levels can be used as a prognostic indicator
- Elevated serum urate concentration may be used to stratify risk of death after acute stroke
- Anti oxidants can be added as a part of treatment protocol in patients with acute ischaemic stroke.

BIBLIOGRAPHY

1. Buettner GR. The pecking order of free radicals and antioxidants: lipid peroxidation, α-tocopherol, and ascorbate. ***Arch Biochem Biophys***. 199-; 300: 535-543.
2. Freedman DS, Williamson DF, Gunter EW, Byers T.Relation of serum urice acid to mortality and ischaemic heart disease. ***Am J Epidemiol.*** 1995; 141: 637-644.
3. The Alpha – Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. ***N Engl J Med***.1994; 330: 1029-1035
4. WHO (1980) Bull WHO 58: 113-130.
5. Plum, F. (1983). What causes infarction in ischaemia brain? The Robert Wartenberg Lecture. ***Neurology*** 33, 222.
6. Leenders, K.A (1983). Experimental aspects of stroke. In ***Vascular disease of the central nervous system*** (ed.R.W.Ros Russell), pp. 73-100.Churchill Livingstone, Edinburgh.
7. Wise, R.J.S.,Bernardi, S.,Frackowiak, R.S.J.,et al.(1983). Serial observations on the Pathophysiology of acute stroke. The transition from ischaemia to infarction as reflected in regional oxygen extraction. ***Brain*** **106**: 197.
8. Cheung, J.Y., Bonventure, J.V., Malis, C.D., and Leaf, A.(1986) Calcium and ischaemia injury. New Engl.J.Med.**314:** 167.
9. Hossman, K.A> (1983). Experimental aspects of stroke. In ***Vascular disease of the central nervous system*** (ed. R.W.Ros Russell), pp. 73-100. Churchill Livingstone, Edinburgh.
10. Lindsberg, P.J., Hallenbeck, J.M.., and feuerstein, G. (1991). Platelet activating factor in stroke and brain injury. ***Ann. Neurol.*** **30**: 117.
11. Stout, R.W.(1989). Hyperglycemia and stroke. Quart. J.med **73,** 997.
12. Becker B.F. et al. Towards the physiological function of uricacid. Free radic boil. Med. 1993. June 14(16) 615-31.
13. Menotti A, Lanti M, Seccareccia F, et al: Multivariate predication of the first major cerebrovascular event in an Italian population sample of middle –aged men followed up for 25 years. Stroke 1993, 24: 42-48.

14. Bonita R, Stewart A.W.Beaglehote R: International trends in stroke mortality. Stroke 1990, 32; 989-992.

15. Sacco RL,Hauser WA, Mohr JP: Hopitalized stroke in blacks and Hispanics in northern Manhattan. Stroke 1991, 22; 1491-1496.

16. Sacco RL,Hauser WA, Mohr JP: One – year outcome after cerebral infarction in whites, blacks and Hispanics. Stroke 1991, 22: 305-311.

17. Yamanouchi H, Shimada H, Kuramoto K: Subtypes and proportions of cerebrovascular disease in an autopsy series in a Japanese geriatric hospital. Kin Wocbenscbr 1990, 68: 1173-1177.

18. Onundarson PT, Thorgerisson G, Jonmundsson, E, et al., chronic atria fibrillation – epidemiological features and 14 years follow – up a case control study, EUr Heart J 1987, 8: 521-527.

19. Feinberg WM, Seeger JF, Carmody RF et al. Epidemiologic features of asymptomatic cerebtal infaction in patients with nonvalvular atria fibrillation. Arcb Intern Med. 1990, 150; 2340-2344.

20. MacMohan S, Cutler JA, Stamler J: Antihydpertensive drug treatment : potrntial, expected, and observed effects on stroke and on coronary heart disease. Hypertension 1989, 13 (suppl): 1-45-1-50.

21. Tanne D, Goldbourt U, Zion M, et al: Frequency and prognosis of stroke/TIA among 4808 survivors of acute myocardial infarction. Stroke 1993, 24: 1490-1495

22. Ellekjaer EF, Wyller TB, Sverre JM, Holmen J: Lifestyle factors and risk of cerebral infarction. Stroke 1992, 23: 829-834.

23. Wolf PA, Belanger AJ, D'Agostino RB: Management of risk factors. ***Neurol Clin*** 1992, 10: 177-191.

24. Barrett-Connor E, Khaw K: Diabetes mellitus: an independent risk factor for stroke. Am J Epidemiol 1988, 128: 116-123.

25. Dennis M, Bamford J, and Sandercock P, warlow C: Prognosis of transient ischaemic attacks in the Oxford shire Community stroke project. Stroke 1990, 21: 848-953.

26. Jamrozik K, Broadhust RJ, Andeson CS, Stewart-Wynne EG: The role of lifestyle factors in the etiology of stroke: a Population –based case-control study in Perth, Western Australia. Stroke 1994; 25: 51-59.

27. Hillbom M, Kaste M; Alcohol abuse and brain infarction. Ann Med. 1990, 22; 347-352.

28. Lindenstrom E, Boysen G, Nyboe J: Lifestyle factors and risk of cerebrovascular disease in women: the Copenhagen city heart study. Stroke 1993, 24: 1468-1472.

29. Fisher CM: Lacunar infarcts: a review, CerebrovascDis 1991,1: 311-320.

30. Bogousslavsky J, Regli F, Maeder P, Meuli R, Nader J: The etiology of posterior circulation infarcts: a prospective study using MRI and MR angiogram. Neurology 1993, 43: 1528-1533.

31. Bogousslavsky J, Van Melle G, Reli F: Middle cerebral Artery – pial territory infarcts: a study of the Lausanne Stroke Registry. Ann Neurol 1989, 25: 555-560.

32. Orgogozo JM, Bogousslavsky J: Lacunar syndromes. In Handbook of Clinical Neurology: Vascular Diseases. Part 2. Edited by Vinken PJ, Bruyb GW, Kalwans HL, Toole JF, Amsterdam: Elsevier Sciences Publishers, 1989: 235-269.

33. Donnan GA, Bladin PF, Berkovic SF, Langley WA, Saling MM: The stroke syndrome of striatocapsular infarction. Brain 1991, 114:51-70.

34. Bogousslavsjy J, Regli F, Maeder P: Intracranial large – artery disease and lacunar infarction. Cerebrovas Dis. 1991, 1: 154-159.

35. Bofousslavsky J, Regli F: Anterior cerebral artery territory infarction in the Lausanne stroke registry: clinical and etiologic patterns. Arcn Neuraol 1990, 47 : 144-150.

36. Solan MA, Haley EC, Jr: The syndrome of bilateral hemisphere border zone ischaemia, Stroke 1990, 21: 1668-1673.

37. Weiller C, Ringelstein EB , Reiche W, Buell U: Clinical and hemodynamic aspects of low –flow infarcts. Stroke 19911, 22: 1117-1123.

38. Bogousslavsky J: The plurality of subcortical infarction. Stroke 1992, 23: 629-631.

39. Amarenco P, Hauw JJ: Cerebellar infarction in the territory of the anterior and inferion cerebellar artery: a clinico-pathological study of 20 cases. Brain 1990, 113: 139-155.

40. Amarenco P, Caplan LR: Vertebrobasilar occlusive disease: Review of selected aspects, 3. Mechanism of cerebellar infarctions. Cerebrovasc Dis. 1993, 3: 66-73.

41. Weingarten K: Computed tomography of cerebral infarction. In neuroimaging clinics of North America. WB Saunders and Co., 1992; 409-419.

42. Wade S. Smith, Stephen L.Hauser, J. Donald Easton. Harrison`s Principles of internal medicine.

PROFORMA

Name	:	Ward No	:
Sex	:	Unit	:
IP No	:	Date of Admission	:
Serial No.	:		
Age	:		
Diabetes	:		
Hypertension	:		
Previous stroke/TIA	:		
Time after stroke onset	:		
Smoking	:		
Fasting Blood Sugar	:		
Blood Pressure	:		
CT	:		
Serum uric acid	:		